

WHAT IS CLAIMED IS:

1. A method for producing motif-specific, context-independent antibodies, said method comprising the steps of:
- (a) constructing a combinatorial peptide library comprising at least one fixed amino acid and surrounding amino acids, wherein at least one surrounding amino acid is variable; and
 - (b) immunizing a host with said peptide library.
2. The method of claim 1, further comprising the steps of isolating the antisera from said host, and purifying said motif-specific, context-independent antibodies from said antisera.
3. The method of claim 1, further comprising the step of utilizing spleen cells from the host of step (b) to generate at least one monoclonal, motif-specific, context-independent antibody.
4. The method of claim 1, wherein said fixed amino acid is a modified amino acid.
5. The method of claim 4, wherein said modified amino acid is selected from the group consisting of a glycosylated amino acid, a phosphorylated amino acid, an acetylated amino acid, a methylated amino acid, a ribosylated amino acid, an isoprenylated amino acid, a lipid-linked amino acid, and an amino acid analog.

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6. The method of claim 1, wherein said fixed amino acid of step (a) is selected from the group consisting of phosphothreonine, phosphoserine, MAPK substrate consensus sites, 14-3-3 consensus binding sites, CDK substrate consensus sites, PKA substrate consensus sites, Akt substrate consensus sites and acetylated lysine.
7. The method of claim 1, wherein said fixed amino acid is an unmodified amino acid.
8. The method of claim 1, wherein said peptide library is between about 6 to 14 amino acids long.
9. A motif-specific, context-independent antibody produced by the method of claims 1, 2 or 3.
10. A motif-specific, context-independent antibody which recognizes at least one fixed amino acid in the context of variable surrounding amino acid or peptide sequences.
11. The motif-specific, context-independent antibody of claim 10, wherein said fixed amino acid is selected from the group consisting of phosphothreonine, phosphoserine, MAPK substrate consensus sites, 14-3-3 consensus binding sites, CDK substrate consensus sites, PKA substrate consensus sites, Akt substrate consensus sites and acetylated lysine.

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12. A method for identifying an unknown substrate of an enzyme, said method comprising the steps of:

- (a) generating at least one motif-specific, context-independent antibody against a motif recognized by said enzyme; and
- (b) screening a target sample with the context-independent antibody for the presence of an unknown substrate containing said motif.

13. The method of claim 12, wherein the motif of step (a) is selected from the group consisting of phosphothreonine, phosphoserine, MARK substrate consensus sites, 14-3-3 consensus binding sites, CDK substrate consensus sites, PKA substrate consensus sites, Akt substrate consensus sites and acetylated lysine.

14. A method for detecting the modification state of a substrate, said method comprising the steps of:

- (a) generating at least one motif-specific, context-independent antibody against a motif selected from the group consisting of an unmodified substrate motif and a modified substrate motif; and
- (b) screening a target sample for the presence of a substrate containing said modification.

15. A method for screening a drug which inhibits or activates enzyme activity on a substrate or a group of substrates, said method comprising the steps of:

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(a) generating at least one motif-specific, context-independent antibody against a motif selected from the group consisting of an unmodified substrate motif and a modified substrate motif; and

(b) screening a target sample treated with said drug for the presence of substrate containing said motif.

16. The method of claim 14 or 15, wherein said motif of step (a) is selected from the group consisting of phosphothreonine, phosphoserine, MAPK substrate consensus sites, 14-3-3 consensus binding sites, CDK substrate consensus sites, PKA substrate consensus sites, Akt substrate consensus sites and acetylated lysine.

17. A method for identifying an enzyme which modifies a known substrate motif, said method comprising the steps of:

(a) generating at least one motif-specific, context-independent antibody against said known substrate motif, wherein said motif is selected from the group consisting of an unmodified substrate motif and a modified substrate motif;

(b) reacting an enzyme sample with said known substrate; and

(c) assaying with the antibody of step (a) for the presence of modified substrate of step (b).

18. The method of claim 17, wherein said motif of step (a) is selected from the group consisting of phosphothreonine, phosphoserine, MAPK substrate consensus sites, 14-3-3

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consensus binding sites, CDK substrate consensus sites, PKA substrate consensus sites, Akt substrate consensus sites and acetylated lysine.

19. A method for profiling protein levels or post-translational modifications in a cell on a genome wide scale, said method comprising the steps of:

- (a) generating at least one motif-specific, context-independent antibody against a conserved substrate motif, wherein said motif is selected from the group consisting of an unmodified substrate motif and a modified substrate motif;
- (b) preparing an extract of said cell; and
- (c) utilizing the antibody of step (a) to profile the levels of one or more proteins containing said motif present in the extract of step (b).

20. The method of claim 19, wherein said motif of step (a) is selected from the group consisting of phosphothreonine, phosphoserine, MAPK substrate consensus sites, 14-3-3 consensus binding sites, CDK substrate consensus sites, PKA substrate consensus sites, Akt substrate consensus sites and acetylated lysine.

21. A method for profiling changes in protein levels or post-translational modifications in a cell on a genome wide scale which result from drug treatment, said method comprising the steps of:

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- (a) generating at least one motif-specific, context-independent antibody against a conserved substrate motif, wherein said motif is selected from the group consisting of an unmodified substrate motif and a modified substrate motif;
- (b) preparing an extract of a cell treated with said drug; and
- (c) utilizing said antibody of step (a) to profile changes in the levels of one or more proteins containing said motif present in said extract of step (b).

22. The method of claim 21, wherein said motif of step (a) is selected from the group consisting of phosphothreonine, phosphoserine, MAPK substrate consensus sites, 14-3-3 consensus binding sites, CDK substrate consensus sites, PKA substrate consensus sites, Akt substrate consensus sites and acetylated lysine.

23. A motif-specific, context-independent antibody which recognizes the substrate consensus sequence for Akt.

24. A motif-specific, context-independent antibody which recognizes the substrate consensus sequence for PKA.

25. A motif-specific, context-independent antibody which recognizes the substrate consensus sequence for bulky ring-directed kinases.

26. The motif-specific, context-independent antibody of claim 25, wherein said consensus sequence for said bulky ring-directed kinase is selected from the group consisting of $[F/4][T/5]^*$ and $[S/T]^*F$.

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